GeneReviews:
A Multi-Authored Online Book

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www.genetests.org

Information resource for healthcare providers to help integrate genetic services into patient care

Located at
University of Washington
Seattle, WA

Funded by
National Institutes of Health

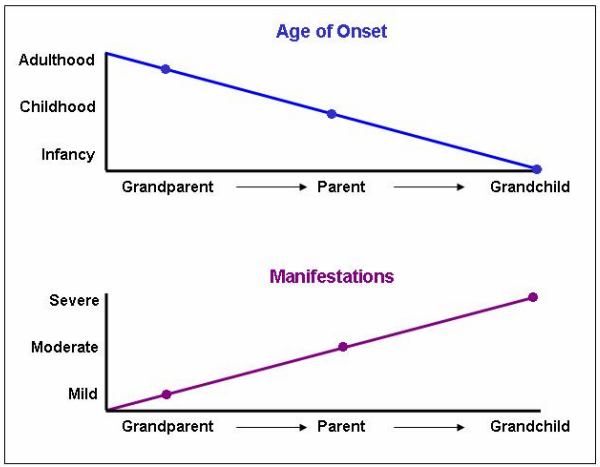
GENETests

Molecular genetic testing for inherited disorders

- **Test menu ever-changing**
  - New genes
  - New test methods
- **Many labs, each testing for a few diseases**
- **Molecular genetic test uses**
  - Medical care
  - Personal decision-making

- ***GeneReviews*:** "User manual" for genetic testing for specific diseases
  - 414 *GeneReviews*
  - One new Review added each week
- **Laboratory Directory:** "Yellow Pages" of genetics labs
  - 615 Clinical and research laboratories
  - >1500 Inherited diseases
- **Clinic D** ...290 res... ...s" of ge...
- **Illustrat** ...counse...

anticipation: The tendency in certain genetic disorders for individuals in successive generations to present at an earlier age and/or with more severe manifestations; often observed in disorders resulting from the expression of a **trinucleotide repeat mutation** that tends to increase in size and have a more significant effect when passed from one generation to the next

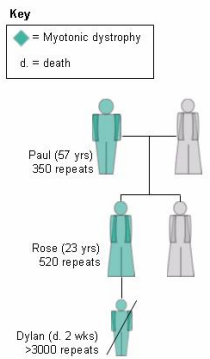


Learn More

Case Example (anticipation): Myotonic dystrophy

Paul is a 57-year-old man with myotonic dystrophy, a neuromuscular disorder caused by a trinucleotide repeat mutation inherited in an autosomal dominant manner. Paul noticed muscle weakness in his late 20s and now has difficulty opening jars and climbing stairs. His 23-year-old daughter, Rose, experienced onset of muscle cramping and weakness as a teenager. Her son, Dylan, born after a pregnancy complicated by polyhydramnios and poor fetal movement, was extremely hypotonic and expired at two weeks of age of respiratory failure. Trinucleotide repeat analysis of the *DMPK* gene reveals that Paul has 350 CTG repeats, Rose has 520 repeats and Dylan over 3000 repeats, consistent with the observed increase in severity of the disorder in subsequent generations.

Case Example



	DMPK gene CTG Repeats	Onset	Clinical Findings
Paul	350	3rd decade	Myotonia, weak facial muscles, general muscle weakness
Rose	520	2nd decade	Myotonia, weak facial muscles, general muscle weakness
Dylan	>3000	Prenatal	Severe weakness, respiratory failure

GeneTests

Online Book

Things to Decide

- Mission
- Audience
- Content & Scope
- Format
- Authoring model
- Editor roles
- Peer review process
- Currency
- Publisher

Online Book
Approach

“Standards emerge from utility”

Jim Ostell 1/24/08

Online Book
Approach

“Standards emerge from utility”

Jim Ostell 1/24/08

Translation:

“At first you just have to wing it”

GeneTests

Mission

Integration of genetic testing into patient care

GeneReviews
Audience

- **Genetics professionals (MD, PhD, MS)**
- **Other healthcare professionals**

- **NOT** the disease expert or lay public

GeneReviews

Content

Disease descriptions focused on use of currently available molecular genetic testing in diagnosis, management, and genetic counseling

GENEReviews

- Allows non-expert clinicians to manage the first encounter with a patient with a given diagnosis
- Correlates information on uses of testing with test availability per GeneTests Laboratory Directory

GENETests

Prader-Willi Syndrome

Molecular Genetic Testing

Test Methods	Mutations Detected	Percent of Individuals
Methylation analysis	Methylation abnormality	99%
FISH / Quantitative PCR	Deletion of PWCR	70%
Uniparental disomy studies	UPD of PWCR	25%
Sequence analysis	Imprinting center defect	<1%

GeneReviews
Format

Highly-structured format for ease of:

- Authoring
- Use at point of care: the “90 second” rule

GeneReviews

GeneReviews
Authoring Model

- Distributed (international)
- Experts MUST include at least one clinician (target audience member)
- Authors use *GeneReviews* template

GeneReviews
Editors

Assure:

- Use of *GeneReviews* format
- Adherence to content/scope requirements
- Consistency with “industry standards” for gene symbol, chromosome locus, protein name, mutation nomenclature

GeneReviews

Peer Review: Internal

- **Clinical geneticists**
  - PubMed search to check content/scope
- **Laboratory geneticists**
  - Mutation nomenclature
  - Test methods consistent with Lab Directory
  - Mutation detection frequency
- **Genetic counselors**
  - Synonyms
  - Standard wording Genetic Counseling section

GeneReviews

Peer Review: External

Purpose

- Accuracy
- Omissions
- Appropriate for target audience

Selection

- Author recommendation
- PubMed search
- Laboratory director

GeneReviews

Updates: Formal review process

Every two years:

- Cancer genetics
- Biochemical genetics
- Treatment/prevention
- Common diseases
- Rapid evolution
- Overviews
- Editor's choice

Every three years: All others

GeneReviews
Updates

Staff

- Incorporates new formatting, style, standard wording
- Reconciles molecular genetic testing with test availability per Laboratory Directory
- Queries authors to clarify existing content
- May or may not perform PubMed search: identifies “hot topics,” organizes by GR TOC

GeneReviews

Updates: PubMed searches

PubMed Search	**Author Expertise**	**Author Understands *GeneReviews***
No	High	Yes
Maybe	High	+/-
Yes	Medium/Low	+/-

GeneReviews
Revisions

- Usually initiated by GeneTests staff when alerted by GeneTests database to new testing listed in Laboratory Directory
- Staff writes suggested wording and propagates necessary changes throughout the GeneReview (e.g., in Diagnosis,Testing Strategy, Genetic Counseling)
- Author edits/approves suggested wording

Online Book
Publisher

- Who will publish?
- Publishing phase requires different technical and editing expertise than content development phase

Online Book

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GeneTests Staff

Principal Investigator **Roberta A Pagon, MD**

GeneReviews

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GENEReviews

Authors

- **No financial compensation**
- **Must**
  - Adhere to *GeneReviews* format, style
  - Reflect clinical test availability as per GeneTests Laboratory Directory
  - Respond to internal and external peer review
- **Term of authorship**
  - Revise when test availability/methods change
  - Update every two to three years

GENETests

Reviewers

- **No financial compensation**
- **Review for:**
  - Accuracy
  - Currency
  - Suitability for healthcare providers